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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,677	07/11/2005	Makoto Shimazaki	BY-RCK-29	1890

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EXAMINER	
AULAKH, CHARANJIT	
ART UNIT	PAPER NUMBER
1625	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,677	SHIMAZAKI ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-26 are pending in the application.

Specification

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight different factors such as quantity of experimentation

necessary, the amount of direction or guidance provided, presence of working examples, state of the prior art, unpredictability and the breadth of claims.

In regard to lack of enablement issue of instant claims 1-26 for derivatives as mentioned on page 24, lines 25-27 (hydrates, solvates or esters) of instant compounds of formula (I), there is no teaching or guidance present in the specification for preparing any specific hydrates (mono, di, tri or tetra), solvates or estrs. Preparation of specific hydrates or solvates of any compound is a very specialized field and involves their characterization using different techniques such as infrared spectrum, XRD powder diffraction etc. There is no teaching or guidance present in the specification regarding any specific solvents used for preparing specific hydrates or solvates and their characterization using any techniques such as XRD powder diffraction or infrared spectrum etc. There is not even a single example present for preparing any specific hydrate or solvate of instant compounds of formula (I). There is lot of unpredictability regarding stability of different hydrates or solvates of any compound in the art. The instant compounds of formula I encompasses hundreds of thousands of compounds based on the values of variables R1-R3, n and m and therefore, in absence of such teachings, guidance, presence of working examples and unpredictability, it would require undue experimentation to select specific hydrates or solvates of instant compounds with enhanced stability properties.

In regard to esters, there is no teaching or guidance present in the specification for preparing specific types of esters such as carboxylic acid esters, amino acid or amide esters, phosphate esters, phosphono esters , sulfate esters etc. There is not even a

single working example present in the specification for preparing any type of specific ester of instant compounds of formula (I). There is lot of unpredictability in the art for efficacy of different types of prodrug forms (esters) of any known compound following their in vivo administration since their efficacy depends upon various factors such as absorption from gut, metabolism by esterases etc. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the values of variables R1-R3, n and m and therefore, in absence of such teachings, guidance, presence of working examples and unpredictability, it would require undue experimentation to select specific types of esters of instant compounds of formula (I) which will be effective following in vivo administration.

In regard to enablement rejection of claims 12-26 for methods of treatment, the specification teaches that the instant compounds are antagonists of Iloprost-induced cAMP production in vitro (see table 1 on pages 34-47 of specification). The specification also mentions that the instant compounds are antagonists of IP receptor and further teaches that IP receptor couples at least to Gs-type G-protein, and activates adenylate cyclase and phospholipase C (see page 1, last two lines). There is no teaching or guidance present in the specification for assessing inhibition of phospholipase C activity by the instant compounds. There is no teaching or guidance present in the specification or prior art that antagonism of only Iloprost-induced cAMP production in vitro is well established model for assessing antagonist activity at IP receptors. There is no teaching or guidance present either in the specification or prior art that hyperactivity of IP receptors is implicated in the etiology of every known

urological disorder, pain, hypotension, hemophilia, hemorrhage and inflammation. There is no teaching in the prior art that structurally closely related compounds having antagonist activity at Iloprost-induced cAMP production in vitro are well known to have therapeutic utility in treating every known urological disorder, pain, hypotension, hemophilia, hemorrhage and inflammation. There are no working examples present showing efficacy of instant compounds in known animal models of every known urological disorder, pain, hypotension, hemophilia, hemorrhage and inflammation. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the values of variables R1-R3, m and n and therefore, in absence of such teachings, guidance, presence of working examples and prior art, it would require undue experimentation to demonstrate efficacy of instant compounds in known animal models every known urological disorder, pain, hypotension, hemophilia, hemorrhage and inflammation and hence their utility for treating these disorders.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-26, the applicants are suggested to delete parenthesis around each claim number and insert a period.

In claim 8, the applicants are suggested to insert a period instead of a semicolon after the last compound.

In claims 9-16, the applicants are suggested to delete ---- medicament ---- and insert ---- A pharmaceutical composition -----.

In claims 22-26, the applicants are suggested to change the term --- process for controlling--- with ---- A method of treating ----.

Claims 17-21 provide for the use of compounds according to claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 17-21 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1 and 9-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Ogilvie (U.S. Patent 6,673,791).

Ogilvie discloses non-nucleoside reverse transcriptase inhibitors for treating HIV. The compound 3003 (see col. 28) disclosed by Ogilvie and pharmaceutical composition containing this compound anticipates the instant claims when R1 represents –OR11 group in the instant compounds of formula (I).

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on (571)272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

C. S. Aulakh

Charanjit S. Aulakh
Primary Examiner
Art Unit 1625